CLAIMS

We claim:

1. A method for diagnosing the presence of, or a predisposition to develop, a fibrotic condition in a patient, wherein said fibrotic condition is other than lung fibrosis, comprising detecting in a biological sample obtained from said patient a target molecule comprising an allele or an expression product thereof, wherein said allele is selected from an allele of a TGF-(beta) gene and an allele of a gene belonging to the same regulatory or biosynthetic pathway as a TGF-(beta) gene, and wherein said allele permits the production of a TGF-(beta) polypeptide at a level and/or functional activity that correlates with the development of said condition.

2. The method of claim 1, wherein said allele is a TGF-(beta)1 allele.

3. The method of claim 2, wherein said TGF-(beta)1 allele comprises a polymorphism within a signal sequence-encoding portion of the allele.

4. The method of claim 2, wherein said TGF-(beta)1 allele encodes an arginine residue at codon 25 relative to the full-length open reading frame of TGF-(beta)1.

5. The method of claim 2, wherein the expression product of said TGF-(beta)1 allele is a polypeptide comprising the sequence set forth in SEQ ID NO: 2.

6. The method of claim 1, wherein said allele of said gene, which belongs to the same regulatory or biosynthetic pathway as the TGF-(beta) gene, is an allele of a gene member of the renin-angiotensin system (RAS).

7. The method of claim 6, wherein said allele permits angiotensin II (AII) to be produced at a level sufficient to induce the production of TGF-(beta)1 at a level and/or functional activity that correlates with the development of said condition.

8. The method of claim 6, wherein said allele is an angiotensinogen (AT) allele.

9. The method of claim 8, wherein said AT allele comprises a polymorphism within its promoter region.

10. The method of claim 8, wherein said AT allele comprises an adenine nucleotide six bases upstream from the transcription start site of AT.

11. The method of claim 8, wherein said AT allele comprises the sequence set forth in SEQ ID NO: 3.

12. The method of claim 1, wherein the fibrotic condition is selected from the group consisting of cardiac fibrosis, kidney fibrosis and hepatic fibrosis.

13. The method of claim 1, wherein the fibrotic condition is a progressive fibrosis

14. The method of claim 1, wherein the fibrotic condition is progressive hepatic fibrosis.

15. The method of claim 1, wherein the patient is infected with chronic hepatitis C virus.

16. A method for diagnosing a higher risk of developing a fibrotic condition in a patient, wherein said fibrotic condition is other than lung fibrosis, comprising detecting in a biological sample obtained from said patient a target molecule comprising an allele or an expression product thereof, wherein said allele is selected from an allele of a TGF-(beta) gene and an allele of a gene belonging to the same regulatory or biosynthetic pathway as a TGF-(beta) gene, wherein said allele correlates with said higher risk.

17. The method of claim 16, wherein said allele is a TGF-(beta)1 allele.

18. The method of claim 17, wherein said TGF-(beta)1 allele comprises a polymorphism within a signal sequence-encoding portion of the allele.

19. The method of claim 17, wherein said TGF-(beta)1 allele encodes an arginine residue at codon 25 relative to the full-length open reading frame of TGF-(beta)1.

20. The method of claim 17, wherein the expression product of said TGF-(beta)1 allele is a polypeptide comprising the sequence set forth in SEQ ID NO: 2.

21. The method of claim 16, wherein said allele of said gene, which belongs to the same regulatory or biosynthetic pathway as the TGF-(beta) gene, is an allele of a gene member of the renin-angiotensin system (RAS).

22. The method of claim 21, wherein said allele permits angiotensin II (AII) to be produced at a level sufficient to induce the production of TGF-(beta)1 at a level and/or functional activity that correlates with the development of said condition.

23. The method of claim 21, wherein said allele is an angiotensinogen (AT) allele.

24. The method of claim 23, wherein said AT allele comprises a polymorphism within its promoter region.

25. The method of claim 23, wherein said AT allele comprises an adenine nucleotide six bases upstream from the transcription start site of AT.

26. The method of claim 23, wherein said AT allele comprises the sequence set forth in SEQ ID NO: 3.

27. The method of claim 16, wherein the fibrotic condition is selected from the group consisting of cardiac fibrosis, kidney fibrosis and hepatic fibrosis.

28. The method of claim 16, wherein the fibrotic condition is a progressive fibrosis

29. The method of claim 16, wherein the fibrotic condition is progressive hepatic fibrosis.

30. The method of claim 16, wherein the patient is infected with chronic hepatitis C virus.

31. A method for diagnosing a lower risk of developing a fibrotic condition in a patient, wherein said fibrotic condition is other than lung fibrosis, comprising detecting in a biological sample obtained from said patient a target molecule comprising an allele or an expression product thereof, wherein said allele is selected from an allele of a TGF-(beta) gene and an allele of a gene belonging to the same regulatory or biosynthetic pathway as a TGF-(beta) gene, wherein said allele correlates with said lower risk.

32. The method of claim 31, wherein said allele is a TGF-(beta)1 allele.

33. The method of claim 32, wherein said TGF-(beta)1 allele comprises a polymorphism within a signal sequence-encoding portion of the allele.

34. The method of claim 32, wherein said TGF-(beta)1 allele encodes a proline residue at codon 25 relative to the full-length open reading frame of TGF-(beta)1.

35. The method of claim 32, wherein said TGF-(beta)1 comprises the sequence set forth in SEQ ID NO: 5.

36. The method of claim 31, wherein said allele of said gene, which belongs to the same regulatory or biosynthetic pathway as the TGF-(beta) gene, is an allele of a gene member of the renin-angiotensin system (RAS).

37. The method of claim 36, wherein said allele permits angiotensin II (AII) to be produced at a level sufficient to induce the production of TGF-(beta)1 at a level and/or functional activity that correlates with the absence of said condition.

38. The method of claim 36, wherein said allele is an angiotensinogen (AT) allele.

39. The method of claim 39, wherein said AT allele comprises a polymorphism within its promoter region.

40. The method of claim 39, wherein said AT allele comprises an guanine nucleotide six bases upstream from the transcription start site of AT.

41. The method of claim 39, wherein said AT allele comprises the sequence set forth in SEQ ID NO: 6.

42. The method of claim 31, wherein the fibrotic condition is selected from the group consisting of cardiac fibrosis, kidney fibrosis and hepatic fibrosis.

43. The method of claim 31, wherein the fibrotic condition is a progressive fibrosis

44. The method of claim 31, wherein the fibrotic condition is progressive hepatic fibrosis.

45. The method of claim 31, wherein the patient is infected with chronic hepatitis C virus.

46. A method for diagnosing a higher risk of developing a fibrotic condition in a patient, wherein said fibrotic condition is other that lung fibrosis, comprising detecting in a biological sample obtained from said patient at least two target molecules selected from different alleles of a TGF-(beta) gene or expression products thereof, and different alleles of a gene belonging to the same regulatory or biosynthetic pathway as a TGF-(beta) gene or expression products thereof, wherein each of said different alleles correlates with said higher risk.

47. The method of claim 46, wherein said alleles are selected from a TGF-(beta)1 allele and an AT allele.

48. The method of claim 47, wherein said TGF-(beta)1 allele encodes an arginine residue at codon 25 relative to the full-length open reading frame of TGF-(beta)1.

49. The method of claim 47, wherein said AT allele comprises an adenine nucleotide six bases upstream from the transcription start site of the AT allele.

50. The method of claim 47, wherein said alleles are present in a homozygous state.

51. The method of claim 46, wherein the fibrotic condition is selected from the group consisting of cardiac fibrosis, kidney fibrosis and hepatic fibrosis.

52. The method of claim 46, wherein the fibrotic condition is a progressive fibrosis

53. The method of claim 46, wherein the fibrotic condition is progressive hepatic fibrosis.

54. The method of claim 46, wherein the patient is infected with chronic hepatitis C virus.

55. A method for diagnosing a lower risk of developing a fibrotic condition in a patient, wherein said fibrotic condition is other that lung fibrosis, comprising detecting in a biological sample obtained from said patient at least two target molecules selected from different alleles of a TGF-(beta) gene or expression products thereof, and different alleles of a gene belonging to the same regulatory or biosynthetic pathway as a TGF-(beta) gene or expression products thereof, wherein each of said different alleles correlates with said lower risk.

56. The method of claim 55, wherein said alleles are selected from a TGF-(beta)1 allele and an AT allele.

57. The method of claim 56, wherein said TGF-(beta)1 allele encodes a proline residue at codon 25 relative to the full-length open reading frame of TGF-(beta)1.

58. The method of claim 56, wherein said AT allele comprises a guanine nucleotide six bases upstream from the transcription start site of the AT allele.

59. The method of claim 56, wherein said alleles are present in a homozygous state.

60. The method of claim 55, wherein the fibrotic condition is selected from the group consisting of cardiac fibrosis, kidney fibrosis and hepatic fibrosis.

61. The method of claim 55, wherein the fibrotic condition is a progressive fibrosis

62. The method of claim 55, wherein the fibrotic condition is progressive hepatic fibrosis.

63. The method of claim 55, wherein the patient is infected with chronic hepatitis C virus.

64. A method for diagnosing an intermediate risk of developing a fibrotic condition in a patient, wherein said fibrotic condition is other than lung fibrosis, comprising detecting in a biological sample obtained from said patient at least two target molecules selected from different alleles of a TGF-(beta) gene or expression products thereof, and different alleles of a gene belonging to the same regulatory or biosynthetic pathway as a TGF-(beta) gene or expression products thereof, wherein at least one of said different alleles correlates with a higher risk of developing said condition and wherein at least one other of said different alleles correlates with a lower risk of developing said condition.

65. The method of claim 64, wherein said alleles that correlate with a higher risk of developing said condition are selected from a TGF-(beta)1 allele that encodes an arginine residue at codon 25 relative to the full-length open reading frame of TGF-(beta)1, and an AT allele that comprises an adenine nucleotide six bases upstream from the transcription start site of the AT allele.

66. The method of claim 64, wherein said alleles that correlate with a lower risk of developing said condition are selected from a TGF-(beta)1 allele that encodes a proline residue at codon 25 relative to the full-length open reading frame of TGF-(beta)1, and an AT allele that comprises a guanine nucleotide six bases upstream from the transcription start site of the AT allele.

67. The method of claim 64, wherein the fibrotic condition is selected from the group consisting of cardiac fibrosis, kidney fibrosis and hepatic fibrosis.

68. The method of claim 64, wherein the fibrotic condition is a progressive fibrosis

69. The method of claim 64, wherein the fibrotic condition is progressive hepatic fibrosis.

70. The method of claim 64, wherein the patient is infected with chronic hepatitis C virus.

71. A method for treating or preventing a fibrotic condition, comprising administering to a patient in need of such treatment an effective amount of an agent, which modulates the level and/or functional activity of an expression product of an allele selected from an allele of a TGF-(beta) gene and an allele of a gene belonging to the same regulatory or biosynthetic pathway as a TGF-(beta) gene, wherein said agent has been identified by a screening process comprising:

contacting a preparation comprising said expression product or a fragment of said expression product or a genetic sequence that modulates the expression of said allele with a test agent; and

detecting a change in the level and/or functional activity of said expression product or said fragment, which is indicative of an agent that is capable of effecting said modulation.

72. The method of claim 71, wherein said allele is a TGF-(beta)1 allele.

73. The method of claim 72, wherein said TGF-(beta)1 allele comprises a polymorphism within a signal sequence-encoding portion of the allele.

74. The method of claim 72, wherein said TGF-(beta)1 allele encodes an arginine residue at codon 25 relative to the full-length open reading frame of TGF-(beta)1.

75. The method of claim 72, wherein the expression product of said TGF-(beta)1 allele is a polypeptide comprising the sequence set forth in SEQ ID NO: 2.

76. The method of claim 71, wherein said allele of said gene, which belongs to the same regulatory or biosynthetic pathway as the TGF-(beta) gene, is an allele of a gene member of the renin-angiotensin system (RAS).

77. The method of claim 76, wherein said allele permits angiotensin II (AII) to be produced at a level sufficient to induce the production of TGF-(beta)1 at a level and/or functional activity that correlates with the development of said condition.

78. The method of claim 76, wherein said allele is an angiotensinogen (AT) allele.

79. The method of claim 78, wherein said AT allele comprises a polymorphism within its promoter region.

80. The method of claim 78, wherein said AT allele comprises an adenine nucleotide six bases upstream from the transcription start site of AT.

81. The method of claim 78, wherein said AT allele comprises the sequence set forth in SEQ ID NO: 3.

82. The method of claim 71, wherein the fibrotic condition is selected from the group consisting of cardiac fibrosis, kidney fibrosis and hepatic fibrosis.

83. The method of claim 71, wherein the fibrotic condition is a progressive fibrosis

84. The method of claim 71, wherein the fibrotic condition is progressive hepatic fibrosis.

85. The method of claim 71, wherein the patient is infected with chronic hepatitis C virus.